VALUE IN HEALTH ▮ (2017) ▮▮▮–▮▮▮

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Cost-Effectiveness of Antibiotic Prophylaxis Strategies for Transrectal Prostate Biopsy in an Era of Increasing Antimicrobial Resistance

Kyueun Lee, MS[1,*], *Dimitri M. Drekonja, MD*[2,3], *Eva A. Enns, PhD*[4]

[1]*Department of Health Research and Policy, School of Medicine, Stanford University, Stanford, CA, USA;* [2]*Minneapolis Veterans Affairs Health Care System, Minneapolis, MN, USA;* [3]*Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota, Minneapolis, MN, USA;* [4]*Division of Health Policy and Management, University of Minnesota School of Public Health, Minneapolis, MN, USA*

ABSTRACT

Objectives: To determine the optimal antibiotic prophylaxis strategy for transrectal prostate biopsy (TRPB) as a function of the local antibiotic resistance profile. **Methods:** We developed a decision-analytic model to assess the cost-effectiveness of four antibiotic prophylaxis strategies: ciprofloxacin alone, ceftriaxone alone, ciprofloxacin and ceftriaxone in combination, and directed prophylaxis selection based on susceptibility testing. We used a payer's perspective and estimated the health care costs and quality-adjusted life-years (QALYs) associated with each strategy for a cohort of 66-year-old men undergoing TRPB. Costs and benefits were discounted at 3% annually. Base-case resistance prevalence was 29% to ciprofloxacin and 7% to ceftriaxone, reflecting susceptibility patterns observed at the Minneapolis Veterans Affairs Health Care System. Resistance levels were varied in sensitivity analysis. **Results:** In the base case, single-agent prophylaxis strategies were dominated. Directed prophylaxis strategy was the optimal strategy at a willingness-to-pay threshold of $50,000/QALY gained. Relative to the directed prophylaxis strategy, the incremental cost-effectiveness ratio of the combination strategy was $123,333/QALY gained over the lifetime time horizon. In sensitivity analysis, single-agent prophylaxis strategies were preferred only at extreme levels of resistance. **Conclusions:** Directed or combination prophylaxis strategies were optimal for a wide range of resistance levels. Facilities using single-agent antibiotic prophylaxis strategies before TRPB should re-evaluate their strategies unless extremely low levels of antimicrobial resistance are documented.

Keywords: antibiotic prophylaxis, cost-effectiveness, directed antibiotic prophylaxis, fluoroquinolone resistance, transrectal prostate biopsy.

Introduction

In 2013, there were 238,590 new prostate cancer diagnoses in the United States, making it the most frequently diagnosed cancer among men [1]. Transrectal prostate biopsy (TRPB) is currently the standard approach to confirm the presence of cancer in men with suspicious prostate neoplasm in case of an abnormal digital rectal examination or elevated prostate-specific antigen test result. TRPB is a frequent urologic procedure, with more than 1 million performed annually in men older than 65 years [2].

TRPB is generally a safe procedure with a low risk of major complications. Nevertheless, postprocedural infections can occur, resulting in fever, urinary tract infection (UTI), or even sepsis. A number of studies of post-TRPB outcomes in North America find hospitalization rates varying from 0% to 6.3% [3,4]. To prevent post-TRPB infections, clinical guidelines recommend the use of antibiotic prophylaxis, predominantly consisting of a course of oral ciprofloxacin taken before the procedure [5].

Despite the initial success in preventing post-TRPB infections with widespread use of antibiotic prophylaxis, rates of postprocedural infectious complications have increased over the past decade [4,6]. Loeb et al. [2] found that hospitalizations due to post-TRPB infections increased from 0.4% in 1991 to 1.2% in 2007 in the United States. Similar trends have been observed in Canada, where the rate of infections per 100 biopsies increased from 0.52 in 2002 to 2009 to 2.15 in 2010 to 2011 [4,6]. There is evidence that these trends are due to increasing levels of fluoroquinolone resistance among enteric bacteria [7–10]. Fecal carriage of fluoroquinolone-resistant *Escherichia coli*, a predominant pathogen in urologic infections, has been found to be significantly associated with sepsis after TRPB [8].

Responses to increasing fluoroquinolone resistance vary. Some facilities have switched to antibiotics with lower rates of antimicrobial resistance in their patient populations [11]. Others have opted for a directed antibiotic strategy, whereby a rectal swab is obtained from each patient and cultured to detect antibiotic-resistant organisms. If resistant organisms are detected,

* *Address correspondence to:* Kyueun Lee, Department of Health Research and Policy, School of Medicine, Stanford University, Redwood Building, T261, Stanford, CA 94305.

E-mail: kyueunl@stanford.edu

1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2017.08.3016

their antibiotic susceptibility profile is used to guide the selection of the prophylactic agent [12]. Nevertheless, costs and benefits of these strategies have not been quantitatively compared in the context of different resistance patterns and it is not clear at which resistance levels a change in prophylaxis policy is warranted. In this study, we sought to evaluate the cost-effectiveness of different prophylaxis strategies to prevent post-TRPB infections and to determine the optimal strategy as a function of the resistance profile of the patient population.

Methods

We developed a decision-analytic model to evaluate the health care costs and quality-adjusted life-years (QALYs) accrued under different antibiotic prophylaxis strategies to prevent post-TRPB infections in a hypothetical cohort of 66-year-old men, the average age of patients undergoing TRPB in a meta-analysis of TRPB outcomes [13]. The model uses a decision tree to estimate the health impacts and mortality risks of possible infectious complications following and the associated health care costs (Fig. 1). Model input parameters were estimated from the published literature and are presented in Table 1. In addition to evaluating outcomes over the first 30 days after TRPB, we evaluated patient costs and QALYs over a lifetime time horizon using a simple state-transition model (Fig. 1) to fully quantify the impact of averting sepsis-related deaths post-TRPB with antibiotic prophylaxis. Both costs and benefits were discounted at 3% per year [14]. All analyses were performed using TreeAge Pro 2013 (TreeAge, Williamstown, MA) [15–29].

Antibiotic Prophylaxis Strategies

We compared four antibiotic prophylaxis strategies: ciprofloxacin alone, ceftriaxone alone, ciprofloxacin and ceftriaxone in combination, and directed therapy based on ciprofloxacin susceptibility testing. We also included a no-prophylaxis strategy in which no antibiotic is administered for comparison in sensitivity analyses. We considered only those strategies involving ciprofloxacin (a fluoroquinolone) as the most commonly used antibiotic class for TRPB prophylaxis and/or ceftriaxone (a cephalosporin) as a promising antibiotic with low levels of resistance [5,30]. In each strategy, antibiotic dosing was assumed to follow recommendations of the American Urological Association: ciprofloxacin was dosed at 500 mg taken orally twice daily for 1 day preprocedure and postprocedure, whereas ceftriaxone was administered as a single 1-2 g intravenous injection 30 minutes before biopsy [5].

Antibiotic Resistance

In the model, we considered bacterial resistance to ciprofloxacin and/or to ceftriaxone. We assumed that resistance to these antibiotics occurs independently. Levels of antibiotic resistance vary across communities and facilities. In the base case, we used the level of ciprofloxacin and ceftriaxone resistance observed in *E. coli* isolates cultured at the Minneapolis Veterans Affairs (VA) Health Care System from July to December 2013. The overall susceptibility profile, which comprises results from diverse clinical samples from both ambulatory and hospitalized patients, was used as a proxy for the prevalence of resistance among patients undergoing TRPB at this facility. We varied the prevalence of resistance in sensitivity analysis.

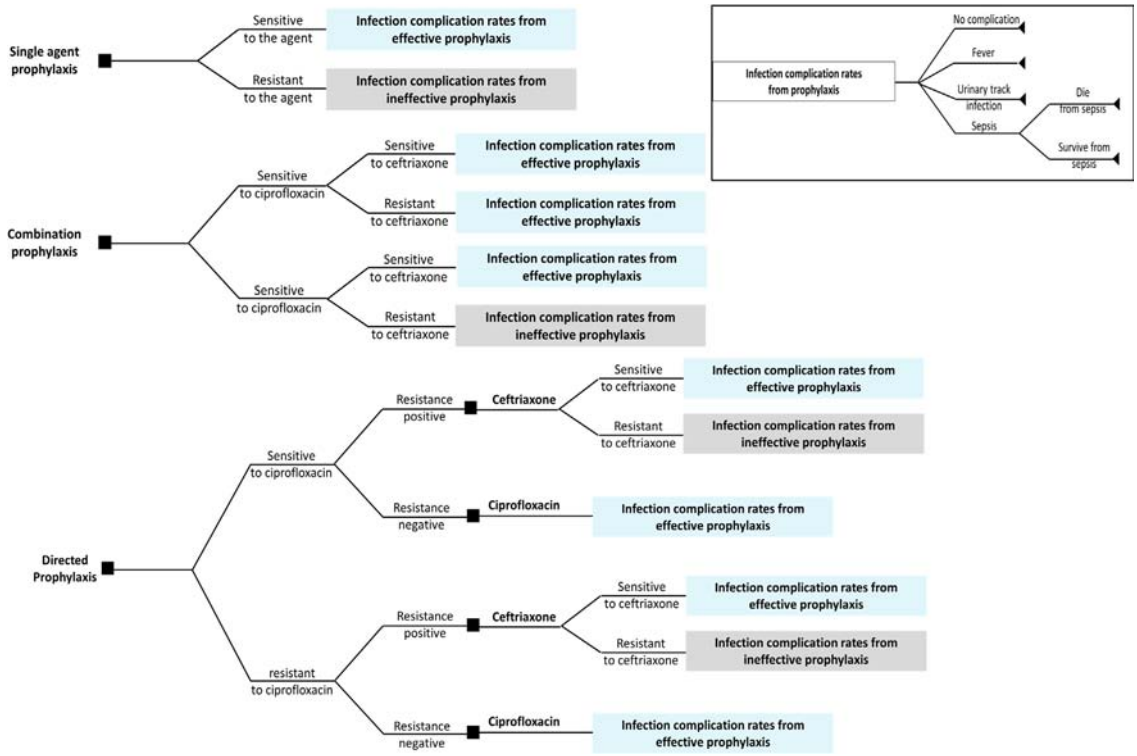

Fig. 1 – A decision tree diagram for antibiotic prophylaxis and infectious complication after TRPB. A single-agent prophylaxis strategy is to treat with either ciprofloxacin or ceftriaxone. Combination prophylaxis is to administer both ciprofloxacin and ceftriaxone. Antibiotic resistance test through rectal swab and culture proceeds antibiotic prophylaxis in directed prophylaxis. Infection complication includes having fever, UTI, fatal or nonfatal sepsis, or no complication, of which rates vary depending on the effectiveness of antibiotic prophylaxis. TRPB, transrectal prostate biopsy; UTI, urinary tract infection.